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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,844	01/13/2006	Eddy Jean Edgard Freyne	JANS-0090	5134

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EXAMINER	
MURRAY, JEFFREY H	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
07/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,844	EDGARD FREYNE ET AL.	
	Examiner	Art Unit	
	Jeffrey H. Murray	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *14-16,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. This action is in response to a response to a restriction requirement filed on June 04, 2007. Applicants' election of Group I is acknowledged. The applicant has selected their election without traverse. There are nineteen claims pending and fourteen under consideration. Claims 14-16, and 18-19 are withdrawn from consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. This is the first action on the merits. The application concerns a novel group of compounds, their use as a medicine, their use for the manufacture of a medicament for the treatment of diseases mediated through glycogen synthase kinase 3 (GSK3), in particular glycogen synthase kinase 3-alpha and 3-beta, processes for their preparation and pharmaceutical compositions comprising them. The restriction requirement is deemed proper and therefore made FINAL.

Priority

2. This application is a non-provisional application 10/564,844, filed January 13, 2006 and is a national stage entry of PCT/EP04/51455, filed July 12, 2004, which claims foreign priority to EP03/50310, filed July 16, 2003. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European Patent Office on July 16, 2003. It is noted, however, that applicant has not filed a certified copy of the EP03/50310 application as required by 35 U.S.C. 119(b).

Specification

3. The abstract of the disclosure is objected to because it exceeds one hundred fifty (150) words, the maximum number it may contain. Correction is required. See MPEP § 608.01(b) and 37 CFR 1.72.

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any of the errors of which applicant may become aware of in the specification.

Claim Objections

5. Claims 1 and 12 are objected to because of the following informalities:

The word "and" needs to be changed to "or" for placing the claim in the alternative format. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-13 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a 3-phenyl or 3-substituted phenyltriazolopyrimidines, does not reasonably provide enablement for triazolopyrimidines that are not substituted by a phenyl group in the 3-position. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (United States v. Teletronics Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See Ex parte Forman 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988).

These factors include the following:

1) *Amount of guidance provided by Applicant.* The Applicant has demonstrated within the application how to make a large number of 3-phenyl or 3-substituted phenyltriazolo-pyrimidines. Within the application, the general formula (I) is a triazolopyrimidine substituted at both the 3- and 5-position. The 5-position is restricted to an amino group directly attached to an A ring, which is restricted to a phenyl, and therefore makes the 5-position a substituted aniline. The 3-position can be substituted with a variety of different radicals, including but not limited to a substituted or non-substituted phenyl ring, a substituted or non-substituted cycloalkyl ring, or a substituted or non-substituted heterocyclic ring. Of the over 330 compounds shown in the current application, only one compound was seen which was not a 3-phenyl or 3-substituted phenyltriazolopyrimidine. This compound, #41, contains a benzyl ring attached directly to the 3-position and refers to a procedure in the specification which demonstrates making a 3-substituted phenyltriazolopyrimidine, so its synthesis remains unclear via the current specification. Of the

rest of these compounds, only a limited number of residue groups are seen on the substituted 3-phenyl group.

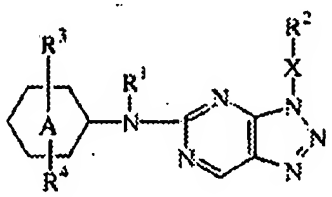
2) *Unpredictability in the art.* It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. (USPQ 18, 24 (CCPA 1970). See *In re Fisher*, 427 F.2d 833, 839, 166. Triazolopyrimidines are currently available drugs for treating depression (antidepressants) such as trazodone; however, tricyclic or similar cyclic anti-depressants have been shown to have side effects such as anticholinergic effects (dry mouth, blurred near vision, constipation, dysuria), antihistamine effects (weight gain, sedation), antiadrenergic effects (postural hypotension, vertigo, dizziness) and cardiotoxicosis or acute poisoning caused by excessive intake. (Nishibe, et. al. US 6,737,085).

The applicants claim in Claim 1 a broad set of triazolopyrimidines with numerous side chains and residue groups. Within the specification, applicants describe in detail the experimental procedure for the preparation of the intermediate and final compounds. Some of the steps within the synthesis stand out as being unpredictable in the potential results that may be observed. For example, in the general synthesis of these triazolopyrimidine compounds, page 26-27 of the specification demonstrates the chloride displacement of the pyrimidine ring by the aniline which will represent the ring A, substituted on the 5-position of the triazolopyrimidine. Here the 3-position portion of the molecule has already been introduced and a reduction and cyclization step are remaining. The reactions following this step involves a reduction of a nitro group to an amino group using platinum (Pt) or palladium (Pd) on carbon, followed by harsh

cyclization conditions whereby the molecule is subjected to a 6 N HCl / glacial acetic acid conditions.

Applicants list that R_2 and R_3 may be substituted by a variety of residue groups such as alkenyl, alkynyl, hydroxyl, cyano, ethers, and other groups. While this may be true, a Pt/C or Pd/C hydrogenation will react to reduce alkenyl or alkynyl groups, (King, et. al. Pt/C; p. 1); (King et. al. Pd/C; p. 1-3), any heterocyclic rings that might be present as R_2 may be substituted in this fashion (King et. al., Pt/C; p. 4), or nitriles (King et. al. Pd/C; p. 3). Likewise, 6 N HCl can react with ethers (Mills, et. al., p. 3) or add to carbon-carbon multiple bonds (Mills, et. al., p.4) as well as react with alcohols (Mills, et. al., p.5). The side chains and residues mentioned above have been shown to contain a degree of uncertainty due to the reagents involved in synthesizing the final compounds.

3) *Scope of the claims*. The scope of the claims involve all of the millions of compounds of general formula (I) where A is phenyl:



Thus, the scope of claims is very broad.

4) *Nature of the invention*. The nature of this invention relates generally to a novel group of compounds, their use as a medicine, their use for the manufacture of a medicament for the treatment of diseases mediated through glycogen synthase kinase 3 (GSK3), in particular glycogen synthase kinase alpha and beta; processes for their preparation and pharmaceutical compositions comprising them.

5) *Level of skill in the art.* The artisan using Applicants invention would be a physician with a M.D. degree, and having several years of experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making these compounds or compositions or treating the diseases mentioned.

Claim Rejections - 35 USC § 112, 2nd

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 12 are only permitted to claim one invention. The language of Claims 1 and 12 are written in such a way as to claim multiple inventions in one claim, which is not permitted. The claims are indefinite and need to be rewritten. Examiner suggests changing the word "and" to "or" in both of the claims.

Conclusion

10. Claims 1-13 and 17 are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on M-F 7:30-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, James Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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